

Rec'd PCT/PTO 12 JAN 2005

INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 03/22181

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/225 A61K31/7068 A61K31/282 A61K31/337 A61K31/415  
A61K31/41 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, CHEM ABS Data, EMBASE, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	REID TONY ET AL: "P1vanex represses oncogene expression and sensitizes tumor cells to chemotherapeutic agents" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 43, March 2002 (2002-03), page 944 XP001154774 93rd Annual Meeting of the American Association for Cancer Research; San Francisco, California, USA; April 06-10, 2002, March, 2002 ISSN: 0197-016X abstract	1-22
Y		1-11, 18, 21, 22
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*A\* document member of the same patent family

Date of the actual completion of the international search

14 November 2003

Date of mailing of the international search report

28/11/2003

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 03/22181

## C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PATNAIK AMITA ET AL: "A phase I study of pivaloyloxymethyl butyrate, a prodrug of the differentiating agent butyric acid, in patients with advanced solid malignancies." CLINICAL CANCER RESEARCH: AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. UNITED STATES JUL 2002, vol. 8, no. 7, July 2002 (2002-07), pages 2142-2148, XP002261509 ISSN: 1078-0432 page 2147, last paragraph	1-11,18, 21,22
X,P	SREEDHARAN SUNIL P ET AL: "Pivanex, a histone deacetylase inhibitor, is synergistic with chemotherapy in inhibiting growth of human non-small cell lung cancer lines." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 44, July 2003 (2003-07), page 742 XP001154773 94th Annual Meeting of the American Association for Cancer Research; Washington, DC, USA; July 11-14, 2003, July 2003 ISSN: 0197-016X abstract	1-5,10, 11,18, 21,22
A	EP 0 302 349 A (UNIV BAR ILAN ;KUPAT HOLIM HEALTH INSURANCE (IL)) 8 February 1989 (1989-02-08) the whole document	1-22
A	CUTTS SUZANNE MARGARET ET AL: "Molecular basis for the synergistic interaction of adriamycin with the prodrug AN-9" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 43, March 2002 (2002-03), page 1087 XP001156158 93rd Annual Meeting of the American Association for Cancer Research; San Francisco, California, USA; April 06-10, 2002, March, 2002 ISSN: 0197-016X cited in the application abstract	1-22

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# INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MARKS P A ET AL: "HISTONE DEACETYLASE INHIBITORS AS NEW CANCER DRUGS"            CURRENT OPINION IN ONCOLOGY, CURRENT SCIENCE LTD, US,            vol. 13, no. 6, 2001, pages 477-483,            XP009010050            ISSN: 1040-8746            page 478; figure 1            page 482, paragraph 2</p>	1-22

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### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 1-21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1, 22 (in part)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 22 (in part)

Present claims 1 and 22 relate to an extremely large number of possible compounds, i.e. inhibitors of histone deacetylase. Support within the meaning of Article 6 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds having formulas I, II, and III and in particular to pivaloyloxymethyl butyrate (claims 2 and 3; examples).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0302349 A	08-02-1989	IL 87072 A	18-08-1993
		AT 95164 T	15-10-1993
		CA 1327595 C	08-03-1994
		DE 3884517 D1	04-11-1993
		DE 3884517 T2	10-02-1994
		EP 0302349 A2	08-02-1989
		ES 2045028 T3	16-01-1994
		HK 1005447 A1	08-01-1999
		JP 1139545 A	01-06-1989
		JP 2763894 B2	11-06-1998
		JP 3044009 B2	22-05-2000
		JP 10152436 A	09-06-1998
		JP 2847078 B2	13-01-1999
		JP 10152454 A	09-06-1998
		US 5200553 A	06-04-1993